

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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|------------------------------|---|----------------------------|
| In re Reissue Application of |) | |
| U.S. Patent No. 4,775,624 |) | |
| |) | |
| Nils U. Bang et al |) | Group Art Unit: 1652 |
| |) | |
| Application No.: 09/185,663 |) | Examiner: William W. Moore |
| |) | |
| Filed: November 4, 1998 |) | |
| |) | |
| For: VECTORS AND COMPOUNDS |) | |
| FOR EXPRESSION OF |) | |
| HUMAN PROTEIN C |) | |

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LETTER TO THE EXAMINER

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

A question has been raised concerning the identity between the Bang et al and Foster et al nucleotide sequences encoding protein C. While the sequences reported in GenBank are identical, two nucleotides have been identified as being different in certain other publications. The Bang et al and Foster et al protein C sequences may be different at the last nucleotide of codon ninety-nine (99) and the last nucleotide of codon two-hundred fourteen (214). All remaining nucleotides of the Bang et al and Foster et al protein C sequences are identical. What is beyond dispute is that all reported sequences encode exactly the same amino acid sequence.

The nucleotide differences between the Bang et al and Foster et al sequences, if there even are such differences, are silent – i.e., the possible differences in the last nucleotide of codon 99 and/or the last nucleotide of codon 214 would not affect the identity of the amino acids encoded by those two codons. Moreover, there is at most a two-nucleotide difference between the Bang et al and the Foster et al sequences out of 1,257 nucleotides (99.84% homology). If the leader sequence of forty-two (42) additional codons is taken into consideration, there is at most a two-nucleotide difference out of 1,383 nucleotides (99.86% homology).

The chart below summarizes information contained in various documents where the Bang et al and Foster et al sequences are disclosed. The paragraphs below compare the documents in such a way as to highlight the similarities and differences at the two nucleotides in question.

| Description | Last Nucleotide of Codon 99 | Last Nucleotide of Codon 214 |
|---|--------------------------------|---------------------------------|
| Bang et al Reissue Application No. 09/185,663 | G | T |
| Bang et al GenBank Sequence X02750 | G | T |
| Foster et al GenBank Sequence nm_000312 | G | T |
| Foster et al '626 Patent (Figure 2*/Figure 3**) | T/T | T/C |
| Foster et al '609 Patent (Figure 2*/Figure 3**) | T/T | T/C |
| Foster et al '529 Patent (Figure 2*/Figure 3**) | T/T | T/C |
| Foster et al PNAS '84 | T | C |
| Foster et al PNAS '85 | T | T |

* Figure 2 is the complete genomic sequence for human protein C.

**Figure 3 is the amino acid and DNA sequence for a cDNA coding for human protein C.

Bang et al Reissue Application Serial No. 09/185,663 and GenBank Sequence X02750

The nucleotide sequence listed in the instant application, Bang et al. reissue application Serial No. 09/185,663 ("the '663 application"), lists "G" at the last nucleotide of codon 99. The '663 application lists "T" at the last nucleotide of codon 214. The Bang et al sequence deposited with GenBank under Accession Number X02750 also lists "G" at the last nucleotide of codon 99 and "T" at the last nucleotide of codon 214 of the '663 application. Therefore, there is absolute similarity between the sequence contained in the '663 application and the GenBank X02750 sequence.

For the Examiner's convenience, pages from the '663 application containing the nucleotide sequence and highlighted at the relevant positions are attached to this Letter at Tab

1. A print-out of the GenBank sequence highlighted at the relevant positions is attached to this Letter at Tab 2.

Bang et al GenBank Sequence X02750 and Foster et al GenBank Sequence nm_000312

The Bang et al GenBank Sequence X02750 and the Foster et al GenBank Sequence nm_000312 (attached at Tab 3) possess the same nucleotide at the last nucleotide of codon 99 and at the last nucleotide of codon 214. Specifically, for both the Bang et al and Foster et al GenBank sequences, the last nucleotide of codon 99 is "G" and the last nucleotide of codon 214 is "T." (See Tabs 2 and 3, respectively) Therefore, there is absolute similarity between the Bang et al GenBank sequence and the Foster et al GenBank sequence.

Foster et al U.S. Patent Nos. 4,968,626; 5,073,609; and 5,302,529
and GenBank Sequence nm_000312

All three Foster patents ("the '626 patent," "the '609 patent," and "the '529 patent;" or "the three Foster patents") contain two Figures which are relevant to this discussion: Figure 2 and Figure 3. Figure 2 is described in each patent as "the complete genomic sequence, including exons and introns, for human protein C." (See, e.g., the '626 patent, column 2, lines 45-46) Figure 3 is described in each patent as "the amino acid and DNA sequence for a cDNA coding for human protein C." (See, e.g., the '626 patent, column 2, lines 55-56)

Figure 2 in all three Foster patents lists "T" at the last nucleotide of codon 99. Figure 3 in all three Foster patents also lists "T" at the last nucleotide of codon 99. However, the Foster et al sequence deposited with GenBank under Accession Number nm_000312 lists "G" at the last nucleotide of codon 99. Therefore, there is no similarity for the last nucleotide of codon 99 between the sequences contained in the '626 patent, the '609 patent, and the '529 patent and the GenBank nm_000312 sequence.

Figure 2 of all three Foster patents lists "T" at the last nucleotide of codon 214. However, Figure 3 of all three Foster patents lists "C" at the last nucleotide of codon 214. Therefore, there is a sequence discrepancy within each of the three Foster patents. Moreover, the Foster et al sequence deposited with GenBank under Accession Number nm_000312 lists "T" at the last nucleotide of codon 214. Only the last nucleotide of codon 214 from Figure 2 of the Foster patents is similar to the last nucleotide of codon 214 from GenBank sequence nm_000312.

For the convenience of the Examiner, pages from the '626 patent containing the nucleotide sequence and highlighted at the relevant positions of Figures 2 and 3 are attached to this Letter at Tab 4. Pages from the '609 patent containing the nucleotide sequence and highlighted at the relevant positions of Figures 2 and 3 are attached to this Letter at Tab 5. Pages from the '529 patent containing the nucleotide sequence and highlighted at the relevant positions of Figures 2 and 3 are attached to this Letter at Tab 6. A print-out of the GenBank

sequence nm_000312 is highlighted at the relevant positions and attached to this Letter at Tab 3.

Foster et al Scientific Articles from 1984 and 1985 and GenBank Sequence nm_000312

Foster et al authored two relevant articles which were published in the Proceedings of the National Academy of Sciences. The first article, published in 1984 ("PNAS '84"), lists "T" at the last nucleotide of codon 99 and "C" at the last nucleotide of codon 214. This information accords with the information listed in Figure 3 of the three Foster patents. The second article, published in 1985 ("PNAS '85"), lists "T" at the last nucleotide of codon 99 and "T" at the last nucleotide of codon 214. This information accords with the information listed in Figure 2 of the three Foster patents.

Neither the PNAS '84 nor the PNAS '85 information for the last nucleotide of codon 99 accords with the information listed in the Foster GenBank nm_000312 sequence corresponding to the last nucleotide for codon 99. Only the PNAS '85 information for the last nucleotide of codon 214 accords with the information listed in the Foster GenBank nm_000312 sequence corresponding to the last nucleotide of codon 214.

For the Examiner's convenience, pages from the PNAS '84 article highlighted at the relevant positions is attached to this Letter at Tab 7. Pages from the PNAS '85 article highlighted at the relevant positions is attached to this Letter at Tab 8.

Application No. 09/185,663
Attorney's Docket No. 008439-016

From the foregoing, further and favorable action in the form of a Notice Declaring Interference is respectfully requested and such action is earnestly solicited.

In the event that there are any questions relating to this letter, or the application in general, it would be greatly appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that the Request for Interference may be expedited.

Respectfully submitted,

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